

Masten.Scott

From: Em.Professor Ian R.Falconer
Sent: Wednesday, August 8, 2001 7:08 AM
To: Scott Masten
Cc: Don Bursill; Andrew Humpage
Subject: NTP recommendation for toxicological studies on cylindrospermopsin

Dear Dr.Masten,

Our research group has been involved in toxicological research into this blue-green algal toxin since 1982. It first came to our attention as the probable cause of poisoning of about 140 children , on Palm Island off the Queensland coast of Australia in 1979.

The first paper is Hawkins et al., 1985. Appl.° Env. Microbiol. 50,1292-1295.

Since that time the chemistry has been unravelled, it is an alkaloid with a hydroxymethyluracil group, and the toxicology has been extended, by several groups including ourselves.

Our most recent research has been in basic toxicology (Falconer et al 1999, Env.Toxicol.14, 143-150), mutagenesis (Humpage et al 2000, Mutation Research 472,155-161) and in oral carcinogenicity°(Falconer et al 2001, Env.Toxicol ,16,192-195.

°We have just concluded a study of oral toxicity to mice over 10 weeks, and are currently in the midst of the histopathology. As far as practicable the OECD protocol was followed. When this data is validated by external referees,it is our intention to provide it to the WHO Chemical Safety Group with respect to a provisional Guideline Value for drinking water.

We have also spent a considerable research effort on the blue-green algal toxin microcystin°(see Humpage et al 2000, J .Toxicol and Env.Health Part A 61,155-165), exploring tumour promotion activity.

We have been considering a major carcinogenesis study of cylindrospermopsin to explore the effects seen in our preliminary work, but will need considerable support and collaboration as our capability does not extend to a study with the extensive protocol of the NTP.

A German group has expressed an interest in collaboration, but we have not made any formal arrangements for joint research or funding at this stage.

We have considerable expertise in the culture characteristics of the organism *Cylindrospermopsis raciborskii* with respect to toxin production, as yet unpublished.We also have experience in bulk purification of toxin, which was required for our oral toxicity study, which is not easy, and toxin analysis.

We have an ongoing research capability within the University of Adelaide and the Cooperative Research Centre for Water Quality and Treatment, but it is not suitable for the very major study protocol required for NTP carcinogenicity testing. We can however undertake elements of such a study with suitable funding support, and will be pleased

to discuss possibilities.

I will be attending the AWWA/WQTC Special Topic day on 14th Nov in Nashville as the opening speaker, so it should be possible to meet at that time.

yours sincerely,

Ian Falconer

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